

In the Claims

Please amend the claims as follows. Applicants present a full set of claims showing markups of the claims with insertions and deletions indicated by underlining and strikethrough text, respectively. The amendments are based on claims filed in the application during the international phase in response to a Written Opinion, which are designated as "original" in this amendment, as contrasted with amended claims ("Currently amended") or new claims ("New").

1. (Currently amended) An *in vitro* method of screening human subjects to assess their risk of developing cervical carcinoma, which method comprises screening the subject for expression of mRNA transcripts of the E6 gene of HPV and sorting the subject into one of two categories of risk for development of cervical carcinoma based on expression of E6 mRNA, wherein individuals positive for expression of E6 mRNA are scored as carrying integrated HPV or a modified episomal HPV genome and are therefore classified as high risk for development of cervical carcinoma, whereas individuals negative for expression of E6 mRNA are scored as not carrying integrated HPV or a modified episomal HPV genome and are therefore classified as no detectable risk for development of cervical carcinoma, characterised in that screening for E6 mRNA expression is carried out using isothermal amplification in combination with real-time detection of the amplification product.

2. (Currently amended) An *in vitro* method of identifying human subjects having abnormal cell changes in the cervix, which method comprises screening the subject for expression of mRNA transcripts of the E6 gene of HPV, wherein individuals positive for expression of E6 mRNA are identified as having abnormal cell changes in the cervix, characterised in that screening for E6 mRNA expression is carried out using isothermal amplification in combination with real-time detection of the amplification product.

3. (Currently amended) A method according to claim 1 ~~or claim 2~~ wherein the isothermal amplification is NASBA, transcription-mediated amplification, signal-mediated amplification of RNA or isothermal solution phase amplification.

4. (Original) A method according to claim 3 wherein screening for E6 mRNA expression is carried out using real-time NASBA.

5. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 4~~ wherein the human subjects are subjects previously identified as infected with human papillomavirus DNA in cells of the cervix.

6. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 5~~ wherein the human subjects are subjects having a previous diagnosis of ASCUS, CIN 1 lesions or condyloma.

7. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 6~~ which comprises screening for E6 mRNA expression using a technique which is able to detect E6 mRNA from at least one cancer-associated HPV type.

8. (Original) A method according to claim 7 which comprises screening for E6 mRNA expression using a technique which is able to detect E6 mRNA from HPV types 16, 18, 31, 33, and preferably 45.

9. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 8~~ wherein individuals positive for expression of E6 mRNA from at least one of HPV types 16, 18, 31, 33 or 45 are scored as carrying integrated HPV.

10. (Original) A kit for use in the detection of mRNA transcripts of the E6 gene(s) of HPV, the kit comprising one or more primer-pairs which enable amplification of a region of E6 transcripts from HPV types 16, 18, 31 and 33 by NASBA and one or more molecular beacon probes.

11. (Original) A kit according to claim 10 which comprises separate primer-pairs specific for each of HPV types 16, 18, 31 and 33.

12. (Currently amended) A kit according to claim 10 ~~or claim 11~~ which comprises one or more of, two or more of and preferably all of the following primer pairs and accompanying identification probes:

5' gatgcaaggctgcatatgagCCACAGGAGCGACCCAGAAA and 5'
AATTCTAATACGACTCACTATAGGGAGAAGGATTCCCATCTCTATATACTA
with probe TATGACTTTTGCTTTTCGGGA;

5' gatgcaaggctgcatatgagGAAAACGATGAAATAGATGGAG and 5'
AATTCTAATACGACTCACTATAGGGAGAAGGGGTCGTCTGCTGAGCTTTCT
with probe GAACCACAACGTCACACAATG;

5' gatgcaaggctgcatatgagACTGACCTCCACTGTTATGA and 5'
AATTCTAATACGACTCACTATAGGGAGAAGGTATCTACTTGTGTGCTCTGT
with probe GGACAAGCAGAACCGGACACATCCAA; and

5' GATGCAAGGTCGCATATGAGTATCCTGAACCAACTGACCTAT and 5'
AATTCTAATACGACTCACTATAGGGAGAAGGTTGACACATAAACGAACTG
with probe GGACAAGCACAACCAGCCACAGC.

13. (New) A method according to claim 2 wherein the isothermal amplification is NASBA, transcription-mediated amplification, signal-mediated amplification of RNA or isothermal solution phase amplification.

14. (New) A method according to claim 13 wherein screening for E6 mRNA expression is carried out using real-time NASBA.

15. (New) A method according to claim 2 wherein the human subjects are subjects previously identified as infected with human papillomavirus DNA in cells of the cervix.

16. (New) A method according to claim 2 wherein the human subjects are subjects having a previous diagnosis of ASCUS, CIN 1 lesions or condyloma.

17. (New) A method according to claim 2 which comprises screening for E6 mRNA expression using a technique which is able to detect E6 mRNA from at least one cancer-associated HPV type.

18. (New) A method according to claim 17 which comprises screening for E6 mRNA expression using a technique which is able to detect E6 mRNA from HPV types 16, 18, 31, 33, and preferably 45.

19. (New) A method according to claim 2 wherein individuals positive for expression of E6 mRNA from at least one of HPV types 16, 18, 31, 33 or 45 are scored as carrying integrated HPV.